

- 10 -

CLAIMS

1. A peptide having, in particular, an antiangiogenic activity, characterized in that it is a cyclized peptide corresponding to the sequence
SEQ ID No 1: X₁X₂RGDX₃FGX₄X₅LLFIHFX₆IGSX₇HSX₈IX₉, in which:
 - the letters without any numerical index correspond to amino acids defined by the single-letter international code,
 - X₁ is either a G or a GG, the amino-terminal end of which is free, alkylated, acylated, or in particular acetylated, or contains a labeling group, such as the biotinyl group,
 - X₂ is either a C, in which case X₂ = X₄, the two Cs then being connected by a disulfide bridge, or X₂ is capable of forming a lactam bridge with X₄, one of X₂ or X₄ being an amino acid bearing an acid group, such as A or D, the other bearing an amino function, such as Q or N,
 - X₃ is either an M motif or a norleucine motif,
 - X₅ is either a motif, or a succession of two di-, tri- or tetrapeptide motifs composed of G or a combination of G and of S, such as GG, GGG, GGGG, GGS, GGGS or GGSGGS, or else X₅ is a C motif, the side chain (thiol function) of which serves as a point for covalent bonding with a 3-nitro-2-pyridinesulfenyl group located on the N-terminal end of the next amino acid (L),
 - X₆ is either an R motif or a K motif,
 - X₇ is either an R motif or a K motif,
 - X₈ is either an R motif or a K motif,
 - X₉ is an aliphatic amino acid (such as G or A), the C-terminal end of which is amidated.
2. The peptide as claimed in claim 1, characterized in that it corresponds to the sequence
SEQ ID No 2: GG*CRGDMFG*CGGLLFIHFRIGSRHSRIG
(*indicates a disulfide bridge connecting the two C

motifs).

3. The peptide as claimed in claim 1 or 2, characterized in that it is modified compared with the native peptide and has, in particular, an alkylated group at its N-terminal end, and/or in that more amino acids are replaced with one or its/their dextrorotary form (_Daa), and/or in that it contains one or more peptide bonds so as to form bioisosters, for example the reduction of an amide bridge to -CH₂NH-, or a retro-inverso reaction.

4. The peptide as claimed in claim 2, in which the RGD motif is exposed via a disulfide bridge between two cysteines, in particular the peptides of sequences SEQ ID No 3 to 10:

SEQ ID No 3: GG*CRGDMFG*CGGLLRIHFRIGSRHSRIG
SEQ ID No 4: GG*CRGDMFG*CGG-LFIHFRIGSRHSRIG
SEQ ID No 5: GG*CRGDMFG*CGGSLFIHFRIGSRHSRIG
20 SEQ ID No 6: GG*CRGDMFG*CGGLLFIHKIGSRHSRIG
SEQ ID No 7: GG*CRGDMFG*CGGLLFIHF^NRIGSRHSRIG
(^NR representing an N-alkylarginine motif)
SEQ ID No 8: GG*CRGDMFG*CGGLLSRHFRIGSRHSRIG
SEQ ID No 9: GG*CRGDMFG*CGGLLSIHFRIGSRHSRIG
25 SEQ ID No 10: GG*CRGDMFG*CGGLLFRHFRIGSRHSRIG.

5. The peptide as claimed in claim 1, characterized in that it contains a sequence

SEQ ID No 11: X-R-G-D-M-F-G-X'
30 exposing the RGD motif via a lactam bridge between the amino acids X (X)-C-O-NH-(X'), X and X' being amino acids such that one bears an acid group and the other bears an amine.

35 6. The peptide as claimed in claim 5, characterized in that it corresponds to the sequences SEQ ID No 12 to SEQ ID No 23:

SEQ ID No 12: GGXRGDMFGX'GGLLFIHFRIGCRHSRIG
SEQ ID No 13: GGXRGDMFGX'GGLLFIFFRIGCRFSRIG

SEQ ID No 14: GGXRGDMFGX'GGLLFIHFRIGSRHSRIG
SEQ ID No 15: GGXRGDMFGX'GGLLRIHFRIGSRHSRIG
SEQ ID No 16: GGXRGDMFGX'GG-LFIHFRIGSRHSRIG
SEQ ID No 17: GGXRGDMFGX'GGSLFIHFRIGSRHSRIG
5 SEQ ID No 18: GGXRGDMFGX'GGLLFIHKIGSRHSRIG
SEQ ID No 19: GGXRGDMFGX'GGLLFIHF^NRIGSRHSRIG
(^NR representing an N-alkylarginine motif)
SEQ ID No 20: GGXRGDMFGX'GGLLSRHFRIGSRHSRIG
SEQ ID No 21: GGXRGDMFGX'GGLLSIHFRIGSRHSRIG
10 SEQ ID No 22: GGXRGDMFGX'GGLLFRHFRIGSRHSRIG
SEQ ID No 23: GGXRGDMFGX'GGLLFIHFRIGSRHSRIG

7. The peptide as claimed in any one of claims 1 to
6, characterized in that it induces apoptosis in human
15 endothelial cells expressing $\alpha V\beta 3$ receptors.

8. The peptide as claimed in any one of claims 1 to
7, characterized in that it undergoes endocytosis by
human endothelial cells expressing $\alpha V\beta 3$ receptors,
20 localizes in the mitochondrial compartment, and exerts
a mitochondriotoxic effect.

9. A pharmaceutical composition, characterized in
that it contains a therapeutically effective amount of
25 at least one peptide as defined in any one of claims 1
to 8, in combination with a pharmaceutically acceptable
vehicle.

30 10. The pharmaceutical composition as claimed in
claim 9, characterized in that it is in the
pharmaceutical form suitable for its administration by
injection, in particular in the form of an injectable
solution for intravenous administration.

35 11. The use of peptides as claimed in any one of
claims 1 to 8, for producing antiangiogenic medicaments
for the treatment of pathologies due to hyper-
vascularization.

12. The use as claimed in claim 11, for producing
medicaments for the treatment of solid tumors such as
pulmonary tumors, adenomas, melanomas, prostate cancer,
breast cancer, colon cancer, pancreatic cancer or
5 osteosarcomas, or the treatment of diabetic
retinopathies and of arthritis.